COMPENDIA TRANSPARENCY TRACKING FORM

DATE: May 31, 2022

OFF-LABEL ID #: 2400

DRUG NAME: Ixazomib

OFF-LABEL USE: AL amyloidosis; Relapsed or refractory, combination therapy

COMPENDIA TRANSPARENCY REQUIREMENTS	
1	Provide criteria used to evaluate/prioritize the request (therapy)
2	Disclose evidentiary materials reviewed or considered
3	Provide names of individuals who have substantively participated in the review or disposition of the request and disclose their potential direct or indirect conflicts of interest
4	Provide meeting minutes and records of votes for disposition of the request (therapy)

EVALUATION/PRIORITIZATION CRITERIA: C, *to meet requirement 1

CODE	EVALUATION/PRIORITIZATION CRITERIA
A	Treatment represents an established standard of care or significant **advance** over current therapies
C	**Cancer** or cancer-related condition
E	Quantity and robustness of **evidence** for use support consideration
L	**Limited** alternative therapies exist for condition of interest
P	**Pediatric** condition
R	**Rare** disease
S	**Serious**, life-threatening condition

Note: a combination of codes may be applied to fully reflect points of consideration [eg, therapy may represent an advance in the treatment of a life-threatening condition with limited treatment alternatives (ASL)]

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Gillmore,J.D., Wechalekar,A., Bird,J., et al: Guidelines on the diagnosis and investigation of AL amyloidosis. Br J Haematol Jan 2015; Vol 168, Issue 2; pp. 207-218.		S
Dispenzieri, A, Kastritis, E, Wechalekar, AD, et al: A randomized phase 3 study of ixazomib-dexamethasone versus physician's choice in relapsed or refractory AL amyloidosis. Leukemia Jan 2022; Vol 36, Issue 1; pp. 225-235.	This was a multi-site open-label randomized Phase 3 trial that investigated ixazomib and dexamethsone in patients with AL amyloidosis. The risk of potential bias associated with randomization, allocation concealment, performance, detection, attrition, and reporting were deemed low. The risk of bias associated with attrition was deemed moderate due to high levels of missing data censoring. No other sources of bias were found.	S
Sanchorawala, V, Palladini, G, Kukreti, V, et al: A phase 1/2 study of the oral proteasome inhibitor ixazomib in relapsed or refractory AL amyloidosis. Blood Aug 03, 2017; Vol 130, Issue 5; pp. 597-605.		2
Cohen, OC, Sharpley, F, Gillmore, JD, et al: Use of ixazomib, lenalidomide and dexamethasone in patients with relapsed amyloid light-chain amyloidosis. Br J Haematol May 2020; Vol 189, Issue 4; pp. 643-649.	This was a retrospective single cohort study that investigated ixazomib, lenalidomide, and dexamethasone combination therapy in patients with light-chain amyloidosis. The risk of bias due to confounding, selection, classification of and deviation from intervention, measurement of outcome, selective reporting, and missing data were deemed low risk. Two major caveats of the study are small sample size and lack of a control group.	S

Hughes, DM, Staron, A, and Sanchorawala, V: A pharmacist's review of the treatment of systemic light chain amyloidosis. J Oncol Pharm Pract Jan 2021; Vol 27, Issue 1; pp. 187-198.		4

Literature evaluation codes: S = Literature selected; 1 = Literature rejected = Topic not suitable for scope of content; 2 = Literature rejected = Does not add clinically significant new information; 3 = Literature rejected = Methodology flawed/Methodology limited and unacceptable; 4 = Other (review article, letter, commentary, or editorial)

CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Megan Smith	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		Todd Gersten	None
		Jeffrey Klein	None
		Richard LoCicero	Incyte Corporation Local PI for REVEAL. Study is a multicenter, non-interventional, non-randomized, prospective, observational study in an adult population for patients who have been diagnosed with clinically overt PV and are being followed in either community or academic medical centers in the US who will be enrolled over a 12-month period and observed for 36 months.

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
IBM MICROMEDEX	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases		B
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The use of Ixazomib in combination therapy to treat amyloidosis demonstrated a moderate degree of benefits in efficacy, with minimal adverse events. The studies were generally small though.	
Todd Gersten	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	In a space where there exists no standard of care options, when compared to other options, the of Ixazomib and dexamethasone significantly improved median time to vital organ deterioration or mortality in a randomized trial. Some data suggests it's most efficacious use may be in combination with lenalidomide as a triplet with dexamethasone.	

Richard LoCicero	Evidence is Inconclusive	Class III: Not Recommended	Insufficient clinical trial data exists to support the routine use of ixazomib in the treatment of relapsed or refractory AL amyloidosis. A phase 3 randomized trial evaluating 168 patients did not meet its primary endpoint. BJH guidelines do not support the use of ixazomib in this setting.	